Huijben et al. (2013) Aggressive chemotherapy and the selection of drug resistant pathogens. *PLoS Pathogens* 9: e1003578

Supporting information

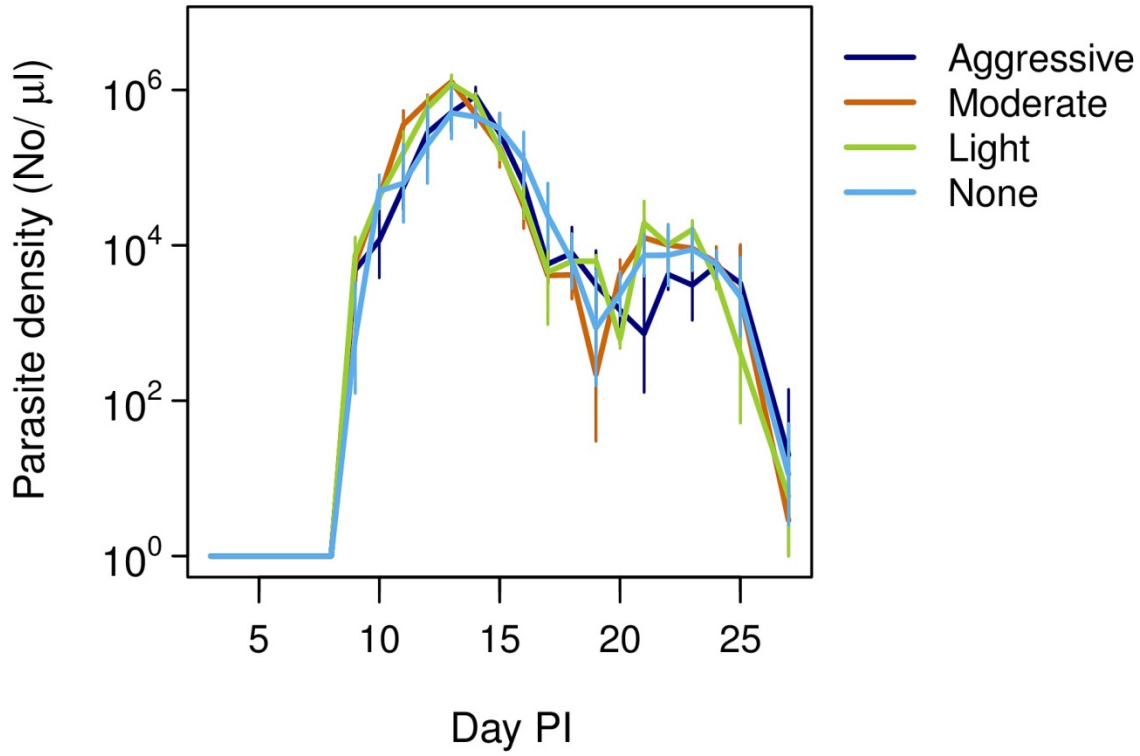

Figure S1.
Parasite dynamics of resistant parasites in single clone infections of experiment 2 following aggressive treatment (dark blue line), moderate treatment (orange line), light treatment (green line) and untreated infections (light blue line). Different drug treatments do not affect the parasite dynamics. Sample sizes as in Table 1.
doi:10.1371/journal.ppat.1003578.s001

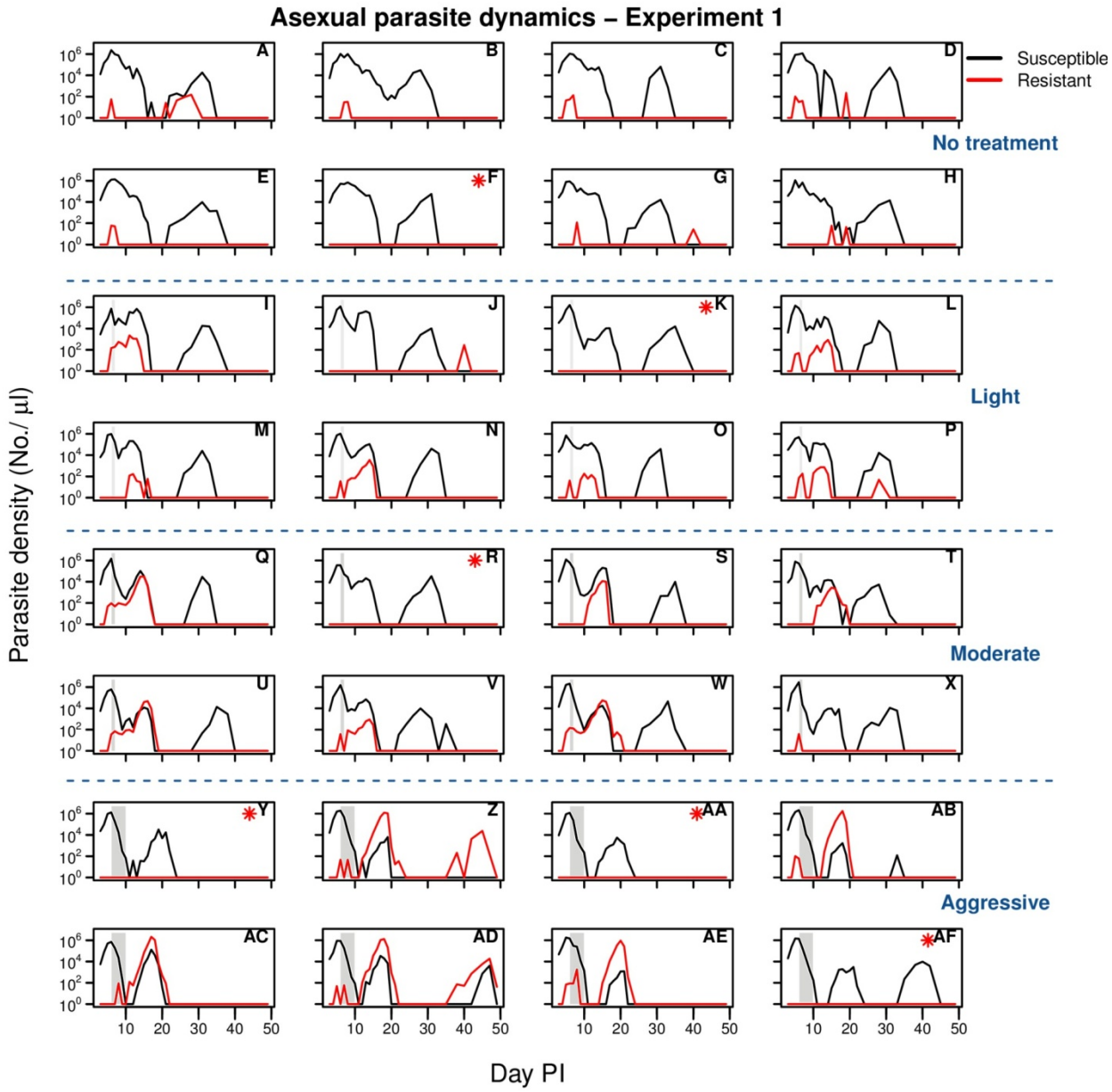

Figure S2.

Asexual parasite dynamics of individual mice in experiment 1 with mixed infections of susceptible (black lines) and resistant (red lines) parasites in untreated infections (A–H), and infections that received a light (I–P), moderate (Q–X) and aggressive (Y-AF) drug treatment (for details, see Table 1). Grey areas show timing and duration of treatment. Asterisks indicate mice that were suspected of not having received resistant parasites as a result of stochastic loss due to low inoculation size and were excluded from the analysis (Table 1).

doi:10.1371/journal.ppat.1003578.s002

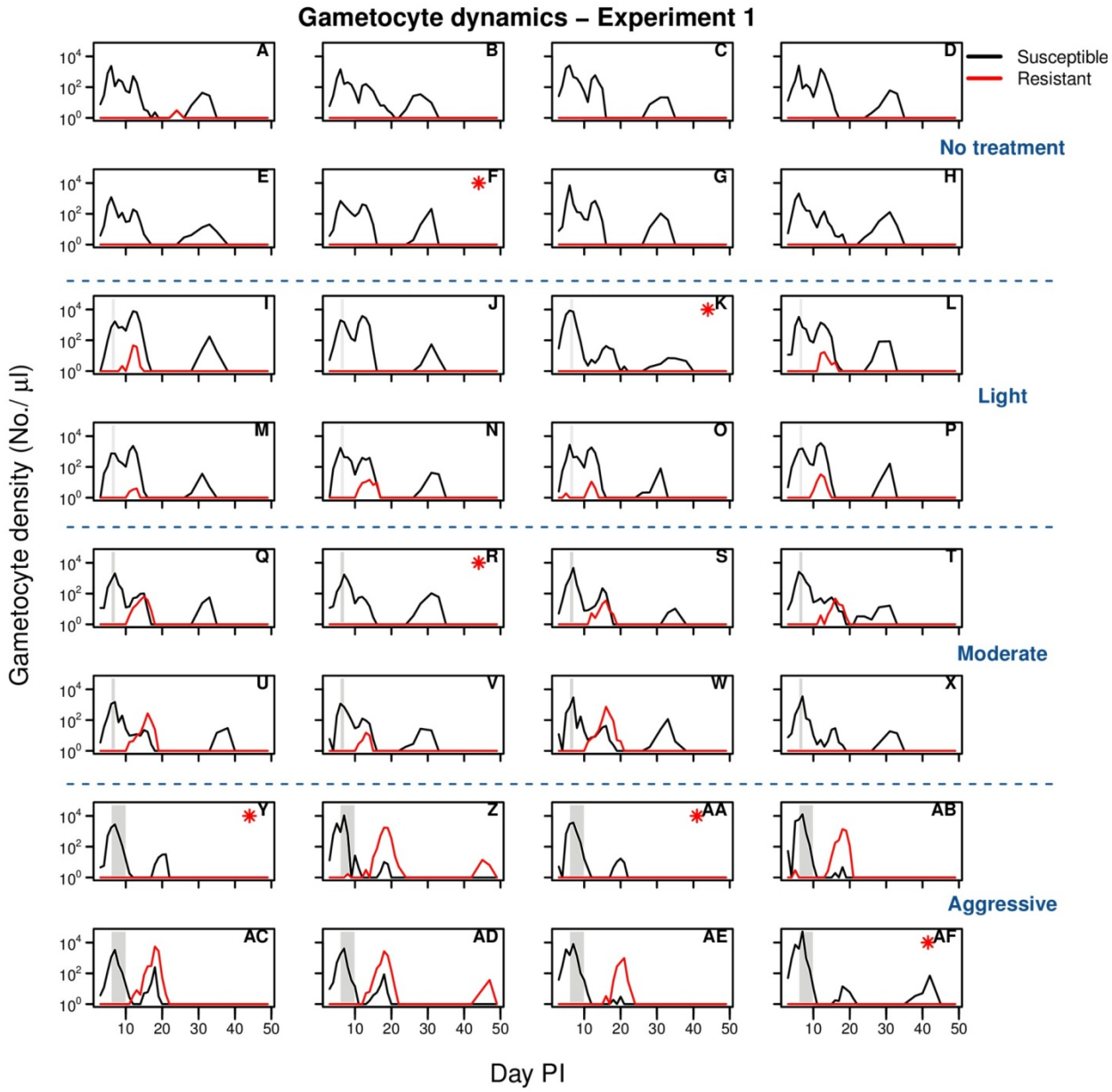

Figure S3.

Gametocyte dynamics of individual mice in experiment 1 with mixed infections of susceptible (black lines) and resistant (red lines) parasites in untreated infections (A–H), and infections that received a light (I–P), moderate (Q–X) and aggressive (Y-AF) drug treatment (for details, seeTable 1). Grey areas show timing and duration of treatment. Asterisks indicate mice that were suspected of not having received resistant parasites as a result of stochastic loss due to low inoculation size and were excluded from the analysis (Table 1).

doi:10.1371/journal.ppat.1003578.s003

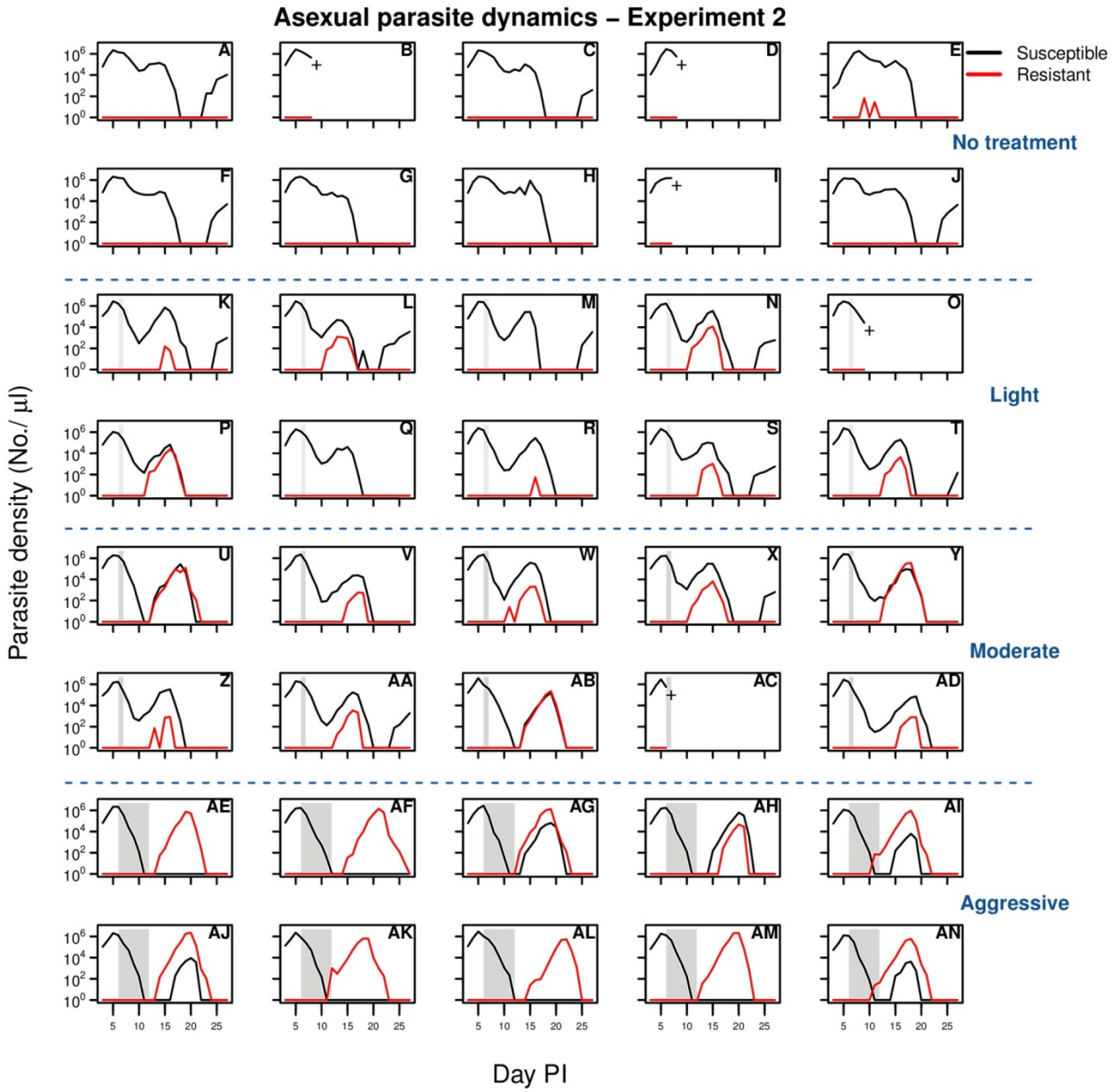

Figure S4.

Asexual parasite dynamics of individual mice in experiment 2 with mixed infections of susceptible (black lines) and resistant (red lines) parasites in untreated infections (A–J), and infections that received a light (K–T), moderate (U-AD) and aggressive (AE-AN) drug treatment (for details, see Table 1). Grey areas show timing and duration of treatment. Crosses indicate mice that died or were euthanized during the infection, asterisks indicate mice that had a lower parasite inoculum than intended. These mice were excluded from the analysis (Table 1).

doi:10.1371/journal.ppat.1003578.s004

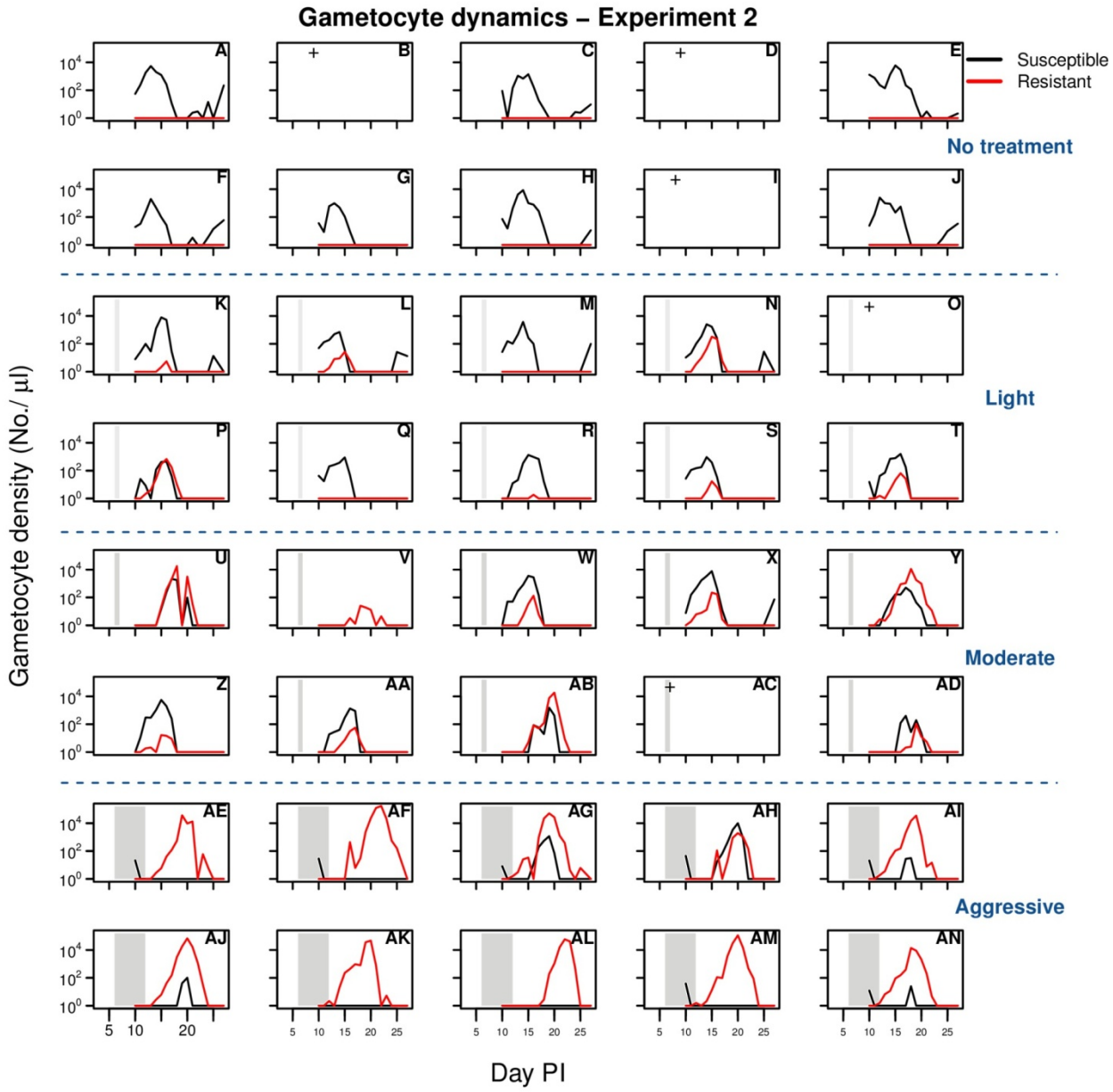

Figure S5.

Gametocyte dynamics of individual mice in experiment 2 with mixed infections of susceptible (black lines) and resistant (red lines) parasites in untreated infections (A–J), and infections that received a light (K–T), moderate (U-AD) and aggressive (AE-AN) drug treatment (for details, seeTable 1). Grey areas show timing and duration of treatment. Crosses indicate mice that died or were euthanized during the infection, asterisks indicate mice that had a lower parasite inoculum than intended. These mice were excluded from the analysis (Table 1).

doi:10.1371/journal.ppat.1003578.s005

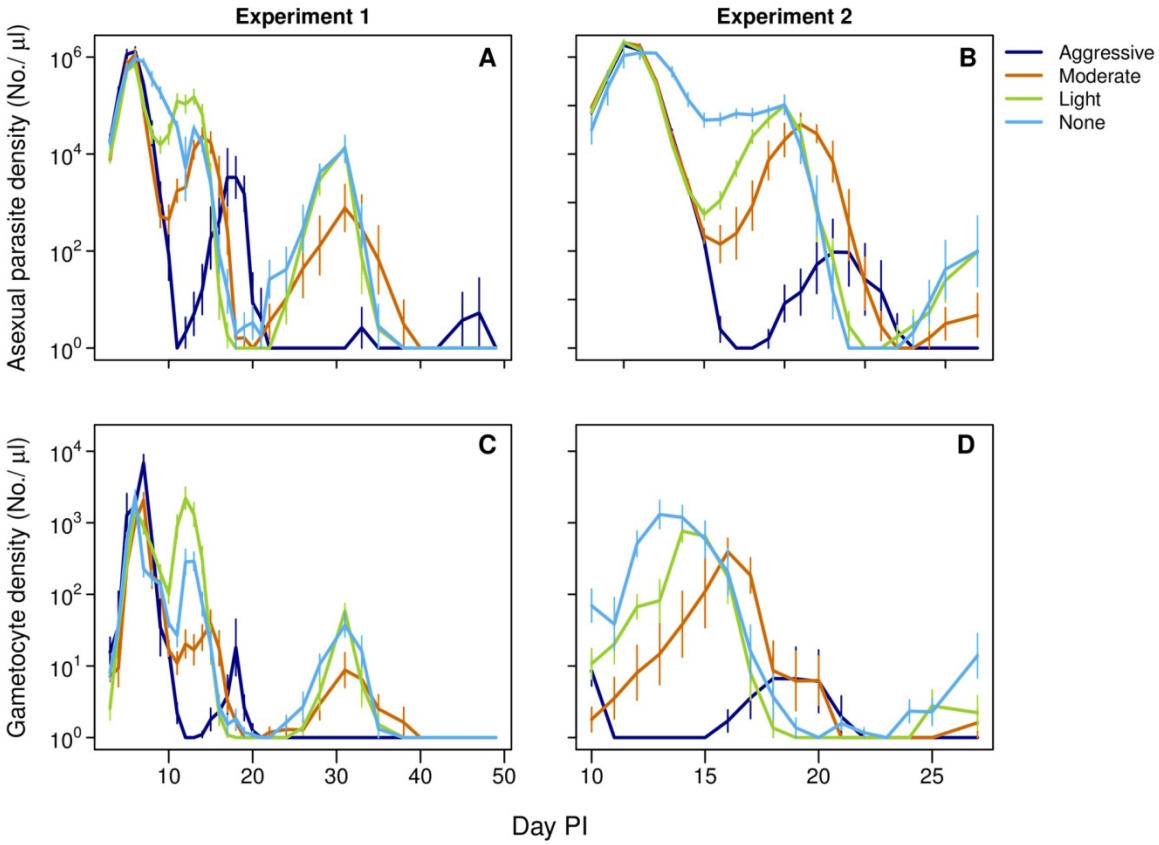

Figure S6.

Mean asexual parasite dynamics (A,B) and gametocyte dynamics (C,D) of the susceptible clone under aggressive (dark blue lines), moderate (orange line), light (green line) or no treatment (light blue line) for experiment 1 (left panels) and experiment 2 (right panels). Data are means (± s.e.m.) with sample sizes as in Table 1. Note experiment 1 and 2 have a different duration of the experiment.

doi:10.1371/journal.ppat.1003578.s006

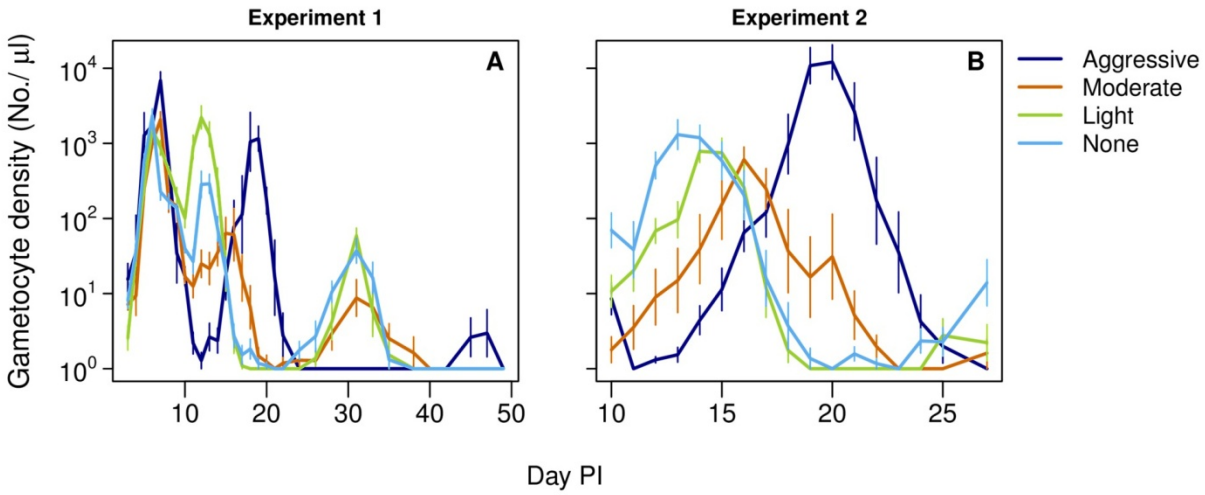

Figure S7.

Mean total gametocyte dynamics (susceptible plus resistant gametocytes) in mixed infections under aggressive (dark blue lines), moderate (orange lines), light (green lines) or no treatment (light blue lines) for experiment 1 (A) and experiment 2 (B). Data are means (± s.e.m.) with sample sizes as in Table 1. Note experiment 1 and 2 have a different duration of experiment.

doi:10.1371/journal.ppat.1003578.s007

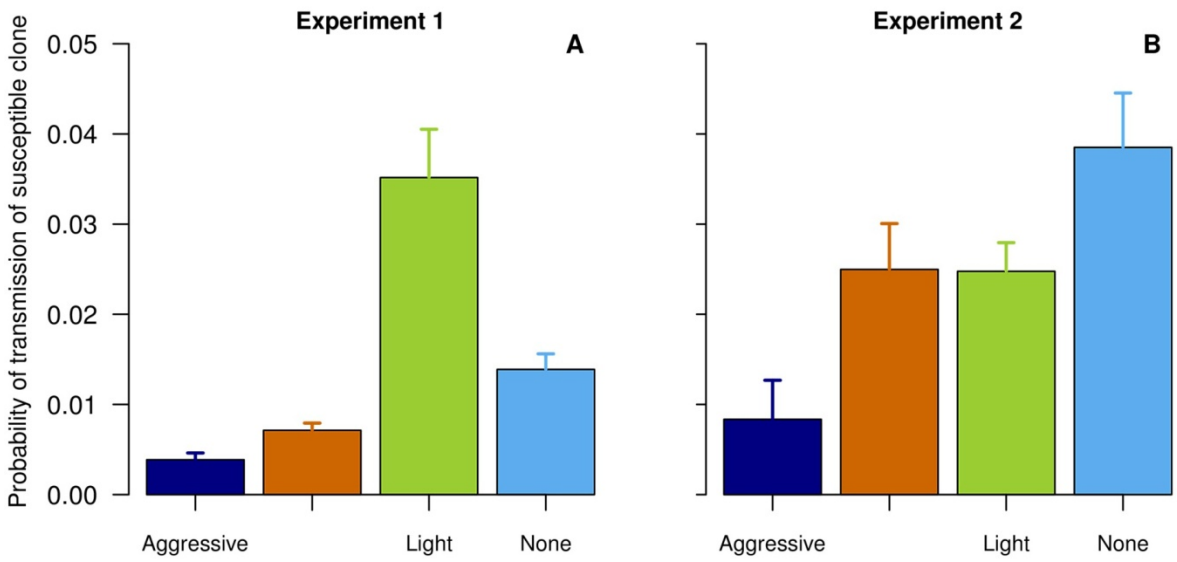

Figure S8.
Probability of infection from the susceptible clone gametocyte density for experiment 1 (A) and experiment 2 (B) based on an established gametocyte density – infectivity relationship (see Materials and Methods) during the relapse period (day 10–28 PI). Data are means (± s.e.m.) with sample sizes as in Table 1.
doi:10.1371/journal.ppat.1003578.s008

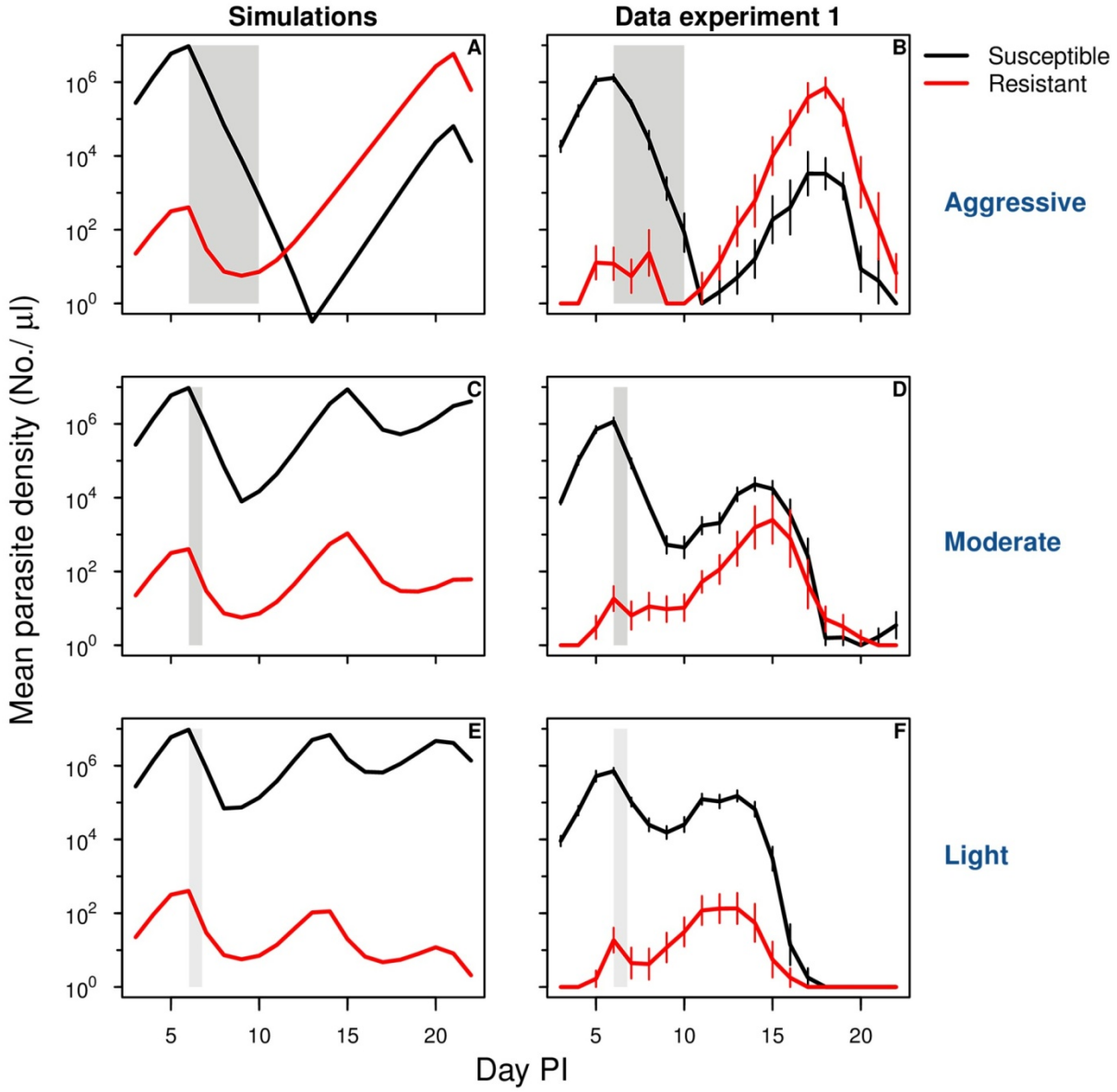

Figure S9.

Drug regimen model simulations (left panels) and experimental data from experiment 2 (right panels) of mixed infections of susceptible (black lines) and resistant (red lines) parasites under aggressive (A,B), moderate (C,D) and light (E,F) treatment regimens. Data in right-hand panels are means (± s.e.m.) with sample sizes as in Table 1. Grey areas demonstrate the timing and duration treatment. Of note is that the model, in contrast to the experimental mice, did not incorporate an immune function to control parasite densities in the later stages of the infection.

doi:10.1371/journal.ppat.1003578.s009